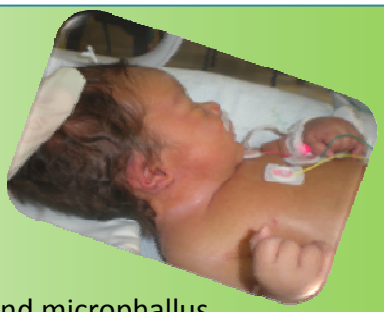
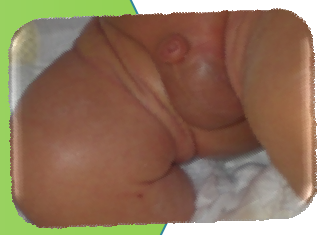
Type 3 Congenital Multiple Pituitary Hormone Deficiency

[a]Radillo L, [a]Fabretto A, [b]Saveanu A, [a]Demarini S, [a]Tonini G, [a]Faleschini E, [a]Tornese G & [a]Pellegrin MC.
[a]Institute for Maternal and Child Health, IRCCS Burlo Garofolo, Trieste, Italy
[b]Unité Mixte de Recherche, Centre de Recherche en Neurobiologie et Neurophysiologie de Marseille, Faculté de Médecine de Marseille, Aix-Marseille Université, Marseille, France
Authors have nothing to disclose

PRENATAL HISTORY
- Prenatal US: **IUGR**, **rhizomelia**, **polihidramnios**
- Amniocentesis: **karyotype 46, XY**





AT BIRTH, at 39 GW by emergency CS:
- weight and lenght <3rd percentile
- head circumference < 10-25th percentile
- Physical examination: short neck, cryptorchidism and microphallus

POSTNATAL PERIOD:
- **early** episode of **hypoglycemia** (20 mg/dl - 1.11 mmol/l) → infusion of D10% through umbelical vein catheter followed by naso-gastric feeding
- **recurrent** episodes of **hypoglycemia** from 8th-14th day of life → corticosteroids
- jaundice with indirect bilirubin in 1st week→ several cycles of **phototherapy**

Hypothesis: CONGENITAL PANHYPOPITUITARISM

INVESTIGATION in the 1st month of life

Laboratory tests	Imaging	Genetics
• **TSH, fT4, fT3 ↓** • **PRL ↓** • **FSH ↓** • **LH ↓** • **GH ↓** • **ACTH, cortisol ↓**	• *CNS US*: normal • *Echocardiography: normal* • *Thorax, abdomen, full skeleton X ray: no evident abnormalities* • *Abdomen US*: mild renal pelvis dilatation, no other abnormalities • *CNS MRI*: no morphologic alterations of pituitary gland and stalk	• gene PROP-1 mutations (cause of CMPHD 2): not found • gene LHX3 mutation (cause of CMPHD 3): **new missense variant (p.Leu196Pro, CTG>GGG) in exon 4 OF lhx3** • No chromosomic anomalies

Recalled at hypothyroidism screening: pathological ABR and diagnosis of bilateral sensorineural hearing loss.

Coexistence of multiple defect of pituitary hormones, short neck, hyposomatotropism and bilateral sensorineural hearing loss make diagnosis of **CONGENITAL MULTIPLE PANHYPOPITUITARISM (CMPHD) associated with LHX3 GENE MUTATION.**
Functional studies demonstrated that this variation determines the inability of the synthesized protein to bind to DNA altering activity of the normal protein.

Because of the same mutation was detected in his mother, asymptomatic, we excluded that this mutation alone is the cause of baby G. panhypopituitarism. SNP's array excluded hemizygosity: **this phenotype may be correlated with a digenic form**.

Now baby G. is treated with L-tiroxina, hydrocortisone and rhGH and underwent bilateral orchidopexy.

Sobrier ML et All. **Symptomatic heterozygotes and prenatal diagnoses in a nonconsanguineous family with syndromic combined pituitary hormone deficiency resulting from two novel LHX3 mutations.** J Clin Endocrinol Metab. 2012 Mar;97(3):E503-9.
Bonfig W, Krude H, Schmidt H. **A novel mutation of LHX3 is associated with combined pituitary hormone deficiency including ACTH deficiency, sensorineural hearing loss, and short neck-a case report and review of the literature.** Eur J Pediatr. 2011 Aug;170(8):1017-21. doi: 10.1007/s00431-011-1393-x. Epub 2011 Jan 20.